**Methods**

Markers for faecal fat estimation in monitoring steatorrhoea in cystic fibrosis

J GILBERT, J KELLEHER, M P WALTERS, AND J M LITTLEWOOD

*From the Regional Cystic Fibrosis Unit and Department of Medicine, St James’s University Hospital, Leeds*

**SUMMARY** Polyethylene glycol (PEG) 4000 is one of numerous substances used as non-absorbable markers to correct for variable faecal output when assessing daily faecal losses of nutrients. The introduction of enteric coated micro-encapsulated pancreatic enzyme (EMPE) preparations has greatly improved the control of fat malabsorption in cystic fibrosis and chronic pancreatitis patients. Unfortunately, these enzyme preparations contain significant quantities of PEG 4000 or polyvinyl pyrolidone (PVP) as components of the enteric coating and thus PEG 4000 cannot be used either as a faecal marker, or in intubation studies, if these enzyme preparations are being used.

Minimising faecal fat output is essential in the management of cystic fibrosis (CF) if the benefits of the high energy, normal fat diet which is now recommended are to be fully realised. Optimal fat balance can only be achieved if faecal fat output is monitored and continuous faecal markers should be used if accurate assessment of faecal fat output is to be obtained. In the past many different substances have been used for this purpose. Polyethylene glycol 4000 is widely used and has been shown to give accurate results for diagnostic purposes in patients not yet receiving treatment. The use of radio-opaque pellets (ROP) has also been advocated on the grounds of simplicity, safety and minimal faecal handling in the laboratory.

It is known that certain oral pharmaceutical preparations contain PEG, and inconsistent results using PEG as a marker in CF patients on a variety of medications lead us to reconsider its value for routine use in this group. We have compared PEG and ROP as continuous faecal markers in CF patients taking EMPE preparations, in doses adjusted according to the fat content of the meal in order to minimise symptoms and faecal fat excretion.

**Methods**

**PATIENTS**

Radio-opaque pellets were prepared by cutting 1.0–1.5 mm lengths of Portex 2.0 mm internal diameter radio-opaque tubing; these were extracted overnight with toluene to remove the plasticiser and, after drying, were packaged in gelatin capsules, each of which contained eight pellets. For seven days 17 CF patients received 500 mg PEG (Sandoz Products Ltd, London) and eight ROP three times daily, and 11 received only eight ROP three times per day. Normal diet and medication were continued throughout the seven days. During the last 48 hours all stools were collected in separate strong polyethylene bags, which fitted directly on to a commode.

Stools were frozen and then x-rayed. Radio-opaque pellets were easily distinguished on x-ray films and were counted. The pooled two day collections were then homogenised and analysis was performed for PEG by the method of Malawer6 and for fat by the method of van de Kamer et al.7

Daily faecal fat output was calculated using each marker.

**Results**

In the CF patients studied, daily faecal fat output ranged from 34.7 mmol to 274 mmol (mean 100.4
mmol) when using ROP as the marker, and from 13·6 mmol to 162·4 mmol (mean 63·2 mmol) when using PEG.

The correlation between PEG and ROP content in the 48 hour faecal collections is shown in the Figure, and it can be seen that despite the close correlation (r=0·87), in all except one of the patients taking pancreatic supplements, there is proportionately more PEG than ROP present. Use of these marker concentrations to calculate daily faecal output results in an error of up to 52% (mean 35%) when PEG was the marker. In the one patient not taking pancreatic supplements, there was only a 6% difference in the results obtained using the two markers.

Two day faecal collections from 11 CF patients taking only ROP as the continuous marker were also analysed for PEG, and contained between 61 mg and 2815 mg of PEG.

The quantity of PEG (or PEG reacting substances) was estimated in a range of medications which are frequently taken by CF patients. These analyses were undertaken on untreated medications and also after incubation with a control faecal homogenate for six hours at 37°C. As seen in the Table, significant quantities of PEG like material were present in many of these preparations. Of particular importance is the large quantity present in each capsule of both Creon (Duphar Laboratories Ltd, Southampon) and Pancrease (Ortho-Cilag Pharmaceutical Ltd, Bucks). Incubation in vitro with a faecal suspension had little effect on the PEG content of Creon or Pancrease, but did reduce considerably the apparent PEG content of the vitamin E suspension and sodium fusidate tablets. The agreement between stated and assayed PEG content of Creon and vitamin E liquid is close in the absence of added faeces. The reduction in apparent PEG content when some of these preparations are incubated with faeces is unexplained.

**Discussion**

Some medications, such as EMPE, which are frequently taken by CF patients, are known to contain PEG or PVP (which will also be determined in the usual turbidimetric method used for PEG analysis). It is also evident that many other medications contain substances which will cause a positive result for PEG and these may be further altered when incubated in faeces. Both the EMPE preparations which are currently available in this country (Creon and Pancrease) contain relatively large quantities of PEG-reacting substances, and some of our CF patients are taking as many as 50 capsules, which
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represents up to 3600 mg of PEG per day. These findings explain the discrepancy between the results obtained using PEG and ROP as markers and the finding of PEG reacting substances in the faeces of patients not taking any PEG as marker.

Polyethylene glycol may be an acceptable marker for diagnostic purposes but cannot be used to monitor treatment of patients taking pancreatic supplementation on certain other medications. Radio-opaque pellets give accurate results in this situation and are easier to estimate.

The range of drugs tested in this study is by no means exhaustive, but the frequency with which PEG like material is found in pharmaceutical preparations suggests that extreme caution should be taken in the interpretation of results where PEG 4000 is used as the continuous non-absorbable marker. The previously used pancreatic enzyme preparations, such as Cotazyme (Organon Laboratories Ltd, Cambridge) and Nutrizyme (Merck Ltd, Alton, Hants), contain much less PEG like material than the newer EMPE preparations.

Radio-opaque pellets have now been used in many thousands of balance studies and harmful side effects have not been described (Cummings J H, personal communication). Our present policy is to use ROP in all patients capable of swallowing a small capsule intact. In younger children, we use a three day collection without any markers.

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References

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